



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 106282

TO: Lawrence E Crane
Location: CM-1/8D14/8B19
Art Unit : 1623
Thursday, October 30, 2003

Case Serial Number: 09/363748

From : Susan Hanley
Location: Biotech-Chem Library
CM1 6B05
Phone: 305-4053

susan.hanley@uspto.gov

Search Notes

Search Request Form

Scientific and Technical Information Center

Requester's Full Name: L. Eric Crane Examiner #: 65753 Date: 10/20/03
Art Unit: 1623 Phone Number: 308-4639 Serial No. 09/363,748
Mail Box & Bldg/Room Loc: 8D-14/CM-1 Results Format Preferred: **PAPER**
[8B-19/CM-1]

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and/or abstract..

Title of Invention: See attached copy of claims.

Inventors (please provide full names): See attached copy of claims.

Earliest Priority Filing Date: 07/31/98

**For Sequence Searches only* Please include all of the pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search for the administration of "a uridine phosphate" (Uridine monophosphate, -diphosphate, -triphosphate, -tetraphosphate, etc. aka UMP, UDP, UTP, etc..) to enhance memory in a host in need thereof. Please also search for a first additional ingredient from the lists found in claims 46, 47 and 48 and a second additional ingredient from the list in claim 49.

STAFF USE ONLY

	Type of Search	Vendors/cost as applicable
Searcher: <u>Hanley</u>	NA Sequence(#) _____	STN _____
Searcher Phone #: _____	AA Sequence(#) _____	Dialog _____
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____
Date Searcher Picked Up: <u>10/23</u>	Bibliographic _____	Dr. Link _____
Date Completed: _____	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Full Text _____	Seq.Syst'ms _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: _____	Other _____	Other(Specify) _____

PT 1 of 2

=> file medline
FILE 'MEDLINE' ENTERED AT 18:21:62 ON 30 OCT 2003

FILE LAST UPDATED: 29 OCT 2003 (20031029/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

CT = controlled terms
NT = narrower term

=> d que 149

```
L1      3391 SEA FILE=REGISTRY ABB=ON  PLU=ON  "URIDINE" AND "PHOSPHATE"
L2      1177 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND NRS=2
L42     2979 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2
L44     45374 SEA FILE=MEDLINE ABB=ON  PLU=ON  MEMORY+NT/CT
L49     2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND L44
```

=> d que 151

```
L1      3391 SEA FILE=REGISTRY ABB=ON  PLU=ON  "URIDINE" AND "PHOSPHATE"
L2      1177 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND NRS=2
L42     2979 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2
L47     10720 SEA FILE=MEDLINE ABB=ON  PLU=ON  MEMORY DISORDERS+NT/CT
L48     30476 SEA FILE=MEDLINE ABB=ON  PLU=ON  ALZHEIMER DISEASE/CT
L51     0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L42 AND (L47 OR L48)
```

TU = therapeutic
AB = admin & dosage
PK = pharmacokinetics
PDE = Pharmacology
AE = adverse effect

=> d que 156

```
L44     45374 SEA FILE=MEDLINE ABB=ON  PLU=ON  MEMORY+NT/CT
L45     24791 SEA FILE=MEDLINE ABB=ON  PLU=ON  URIDINE+NT/CT
L46     9733 SEA FILE=MEDLINE ABB=ON  PLU=ON  URACIL NUCLEOTIDES+NT/CT
L47     10720 SEA FILE=MEDLINE ABB=ON  PLU=ON  MEMORY DISORDERS+NT/CT
L48     30476 SEA FILE=MEDLINE ABB=ON  PLU=ON  ALZHEIMER DISEASE/CT
L53     10243 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L45 OR L46)(L)(TU OR AD OR
      PK OR PD OR AE)/CT
L54     12 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L44 OR (L47 OR L48)) AND L53
L55     11 SEA FILE=MEDLINE ABB=ON  PLU=ON  L54 AND (MEMORY OR LEARN?)
L56     4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L55 AND ?PHOSPHATE
```

=> s 149 or 151 or 156

L94 5 L49 OR L51 OR L56 5 cites from medline

=> file drugu

FILE 'DRUGU' ENTERED AT 18:21:05 ON 30 OCT 2003
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FILE LAST UPDATED: 23 OCT 2003 <20031023/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001. <<<
>>> (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION <<<
>>> SEE HELP COST <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

=> d que 165

L63 269 SEA FILE=DRUGU ABB=ON PLU=ON (URIDIN? OR URACIL)(5A)(PHOSPHAT
E OR MONOPHOSPH? OR DIPHOSPH? OR TRIPHOSPH?)
L64 13997 SEA FILE=DRUGU ABB=ON PLU=ON MEMORY OR LEARNING OR COGNIT?
OR AMNESI?
L65 0 SEA FILE=DRUGU ABB=ON PLU=ON L63 AND L64

no cites from drug u

=> file embase

FILE 'EMBASE' ENTERED AT 18:21:07 ON 30 OCT 2003
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FILE COVERS 1974 TO 30 Oct 2003 (20031030/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d que 174

L66 169222 SEA FILE=EMBASE ABB=ON PLU=ON MEMORY OR LEARNING OR COGNIT?
OR AMNESI?
L67 7755 SEA FILE=EMBASE ABB=ON PLU=ON (URIDIN? OR URACIL)(5A)(PHOSPHA
TE OR MONOPHOSPH? OR DIPHOSPH? OR TRIPHOSPH?)
L68 22 SEA FILE=EMBASE ABB=ON PLU=ON L66 AND L67
L69 645 SEA FILE=EMBASE ABB=ON PLU=ON URIDINE PHOSPHATE/CT
L70 729 SEA FILE=EMBASE ABB=ON PLU=ON URIDINE DIPHOSPHATE/CT
L71 2246 SEA FILE=EMBASE ABB=ON PLU=ON URIDINE TRIPHOSPHATE/CT
L73 390 SEA FILE=EMBASE ABB=ON PLU=ON (L69 OR L70 OR L71)(L)(PD OR
DO OR DV OR TU)/CT
L74 3 SEA FILE=EMBASE ABB=ON PLU=ON L73 AND L68

*PD = pharmacology
DO = dosage
DV = drug development
TV = therapy*

=> d que 183

L66 169222 SEA FILE=EMBASE ABB=ON PLU=ON MEMORY OR LEARNING OR COGNIT?
OR AMNESI?
L69 645 SEA FILE=EMBASE ABB=ON PLU=ON URIDINE PHOSPHATE/CT
L70 729 SEA FILE=EMBASE ABB=ON PLU=ON URIDINE DIPHOSPHATE/CT
L71 2246 SEA FILE=EMBASE ABB=ON PLU=ON URIDINE TRIPHOSPHATE/CT
L75 7418 SEA FILE=EMBASE ABB=ON PLU=ON CHOLINE/CT
L77 3272 SEA FILE=EMBASE ABB=ON PLU=ON SPHINGOMYELIN/CT
L78 6969 SEA FILE=EMBASE ABB=ON PLU=ON LECITHIN
L79 1111 SEA FILE=EMBASE ABB=ON PLU=ON LYSOLECITHIN
L81 4760 SEA FILE=EMBASE ABB=ON PLU=ON PHOSPHATIDYLETHANOLAMINE/CT
L82 48 SEA FILE=EMBASE ABB=ON PLU=ON L66 AND (L75 OR (L77 OR L78 OR
L79) OR L81)(L)(TU OR PD OR DO OR DV OR DC)/CT
L83 1 SEA FILE=EMBASE ABB=ON PLU=ON L82 AND (L69 OR L70 OR L71)

*DC = drug
comparison*

=> d que 189

L66 169222 SEA FILE=EMBASE ABB=ON PLU=ON MEMORY OR LEARNING OR COGNIT?
OR AMNESI?
L86 827 SEA FILE=EMBASE ABB=ON PLU=ON PHOSPHORYLASE(5A)INHIBIT?
L87 102 SEA FILE=EMBASE ABB=ON PLU=ON URIDINE(5A)(RENAL OR SECRET?
OR COMPET?)
L88 2 SEA FILE=EMBASE ABB=ON PLU=ON (L86 OR L87) AND L66
L89 0 SEA FILE=EMBASE ABB=ON PLU=ON L88 AND (URIDINE OR URACIL)

=> s 174 or 183 or 189

L95

3 L74 OR L83 OR L89

3 cites for embase

=> file hcaplus

FILE 'HCAPLUS' ENTERED AT 18:21:09 ON 30 OCT 2003
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FILE COVERS 1907 - 30 Oct 2003 VOL 139 ISS 18
 FILE LAST UPDATED: 29 Oct 2003 (20031029/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 114

L1	3391	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	"URIDINE" AND "PHOSPHATE"
L2	1177	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	L1 AND NRS=2
L3	10669	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L2
L4	1095	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L3(L)(THU OR PKT OR PAC OR DMA OR BAC)/RL
L9	1475	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	AMNESIA/CT
L10	30335	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	MENTAL ACTIVITY+PFT,NT/CT
L14	2	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	(L9 OR L10) AND L4

*PFT = old, new or
"used for" terms*

*THU = therapy
PKT = pharmacokinetics*

*PAC = pharmacol.
DMA = drug
mechanism of action*

BAC = Biol. action

=> d que 121

L1	3391	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	"URIDINE" AND "PHOSPHATE"
L2	1177	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	L1 AND NRS=2
L9	1475	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	AMNESIA/CT
L10	30335	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	MENTAL ACTIVITY+PFT,NT/CT
L15	20	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L2 AND (L9 OR L10)
L21	11	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L15 AND MEMORY

=> d que 123

L1	3391	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	"URIDINE" AND "PHOSPHATE"
L2	1177	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	L1 AND NRS=2
L3	10669	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L2
L4	1095	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L3(L)(THU OR PKT OR PAC OR DMA OR BAC)/RL
L11	2285	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	COGNITION ENHANCERS+PFT/CT
L12	3634	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	"ANTI-ALZHEIMER'S AGENTS"/CT
L23	2	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L4 AND (L11 OR L12)

ring systems = NRS

=> d que 129

L5	1184	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	PYRIMIDINE NUCLEOSIDES+PFT/CT
L7	1057	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	PYRIMIDINE NUCLEOTIDES+PFT/CT

L9 1475 SEA FILE=HCAPLUS ABB=ON PLU=ON AMNESIA/CT
 L10 30335 SEA FILE=HCAPLUS ABB=ON PLU=ON MENTAL ACTIVITY+PFT,NT/CT
 L27 5 SEA FILE=HCAPLUS ABB=ON PLU=ON (L5 OR L7) AND (L9 OR L10)
 L28 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND (?URIDIN? OR ?URACIL?)
 L29 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 NOT (METHYLGLUCAMINE)/TI

=> d que 135

L1 3391 SEA FILE=REGISTRY ABB=ON PLU=ON "URIDINE" AND "PHOSPHATE"
 L2 1177 SEA FILE=REGISTRY ABB=ON PLU=ON L1 AND NRS=2
 L3 10669 SEA FILE=HCAPLUS ABB=ON PLU=ON L2
 L9 1475 SEA FILE=HCAPLUS ABB=ON PLU=ON AMNESIA/CT
 L10 30335 SEA FILE=HCAPLUS ABB=ON PLU=ON MENTAL ACTIVITY+PFT,NT/CT
 L11 2285 SEA FILE=HCAPLUS ABB=ON PLU=ON COGNITION ENHANCERS+PFT/CT
 L12 3634 SEA FILE=HCAPLUS ABB=ON PLU=ON "ANTI-ALZHEIMER'S AGENTS"/CT
 L13 44995 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHATIDYLCHOLINES+PFT,NT/CT
 L34 91 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND (L9 OR L10 OR L11 OR L12)
 L35 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND L3

=> d que 136

L5 1184 SEA FILE=HCAPLUS ABB=ON PLU=ON PYRIMIDINE NUCLEOSIDES+PFT/CT
 L7 1057 SEA FILE=HCAPLUS ABB=ON PLU=ON PYRIMIDINE NUCLEOTIDES+PFT/CT
 L9 1475 SEA FILE=HCAPLUS ABB=ON PLU=ON AMNESIA/CT
 L10 30335 SEA FILE=HCAPLUS ABB=ON PLU=ON MENTAL ACTIVITY+PFT,NT/CT
 L11 2285 SEA FILE=HCAPLUS ABB=ON PLU=ON COGNITION ENHANCERS+PFT/CT
 L12 3634 SEA FILE=HCAPLUS ABB=ON PLU=ON "ANTI-ALZHEIMER'S AGENTS"/CT
 L13 44995 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHATIDYLCHOLINES+PFT,NT/CT
 L34 91 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND (L9 OR L10 OR L11 OR L12)
 L36 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND (L5 OR L7)

=> d que 137

L9 1475 SEA FILE=HCAPLUS ABB=ON PLU=ON AMNESIA/CT
 L10 30335 SEA FILE=HCAPLUS ABB=ON PLU=ON MENTAL ACTIVITY+PFT,NT/CT
 L11 2285 SEA FILE=HCAPLUS ABB=ON PLU=ON COGNITION ENHANCERS+PFT/CT
 L12 3634 SEA FILE=HCAPLUS ABB=ON PLU=ON "ANTI-ALZHEIMER'S AGENTS"/CT
 L13 44995 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHATIDYLCHOLINES+PFT,NT/CT
 L34 91 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 AND (L9 OR L10 OR L11 OR L12)
 L37 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND (?URIDIN? OR ?URACIL?)

=> s l14 or l21 or l23 or l29 or l35-37

L96 18 L14 OR L21 OR L23 OR L29 OR (L35 OR L36 OR L37)

=> dup rem 194 165 195 196

L65 HAS NO ANSWERS

FILE 'MEDLINE' ENTERED AT 18:21:52 ON 30 OCT 2003

FILE 'EMBASE' ENTERED AT 18:21:52 ON 30 OCT 2003

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PROCESSING COMPLETED FOR L94

PROCESSING COMPLETED FOR L65

PROCESSING COMPLETED FOR L95

PROCESSING COMPLETED FOR L96

L97 24 DUP REM L94 L65 L95 L96 (2 DUPLICATES REMOVED) *24 cites*

ANSWERS '1-5' FROM FILE MEDLINE

ANSWERS '6-8' FROM FILE EMBASE

ANSWERS '9-24' FROM FILE HCAPLUS

=> d ibib abs ind 1

L97 ANSWER 1 OF 24 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 78245511 MEDLINE
DOCUMENT NUMBER: 78245511 PubMed ID: 682696
TITLE: Retention improvement by topical application of uridine
monophosphate into different brain areas.
AUTHOR: Ott T; Grecksch G; Matthies H
SOURCE: MEDICAL BIOLOGY, (1978 Jun) 56 (3) 133-7.
Journal code: 0417300. ISSN: 0302-2137.
PUB. COUNTRY: Finland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197810
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19970203
Entered Medline: 19781027

AB This study aimed to demonstrate the effect of uridine monophosphate (UMP) on the consolidation of a brightness-discrimination reaction after topical application of this RNA precursor into the hippocampus, the neocortex or the mesencephalic reticular formation (MRF). Thirty minutes before the rats started their training in a Y-chamber, UMP was injected into each animal through cannula implanted into the particular brain area. When injected into hippocampus or MRF UMP exerted no influence on acquisition, but after epidural UMP injection an impairment of acquisition was observed. After intrahippocampal or epidural UMP application the retention test carried out 48 hour after training showed a significant improvement in retention performance, whereas UMP injection into MRF showed no influence on retention. Consequently, the retention-improving effect of UMP is probably not induced by activation of ascending neuronal systems.

CT Check Tags: Animal; Comparative Study; Male
Administration, Topical
Behavior, Animal: DE, drug effects
*Brain: DE, drug effects
Cerebral Cortex: DE, drug effects
Conditioning (Psychology): DE, drug effects
Hippocampus: DE, drug effects
Learning: DE, drug effects
*Memory: DE, drug effects
Mesencephalon: DE, drug effects
Rats
*Retention (Psychology): DE, drug effects
Reticular Formation: DE, drug effects
*Uracil Nucleotides: PD, pharmacology
Uridine Monophosphate: AD, administration & dosage
*Uridine Monophosphate: PD, pharmacology
RN 58-97-9 (Uridine Monophosphate)
CN 0 (Uracil Nucleotides)

=> d ibib abs ind 2-5

L97 ANSWER 2 OF 24 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 73207466 MEDLINE
 DOCUMENT NUMBER: 73207466 PubMed ID: 4714676
 TITLE: Suppression of uridine monophosphate-induced
 improvement in long-term storage by cycloheximide.
 AUTHOR: Ott T; Matthies H
 SOURCE: PSYCHOPHARMACOLOGIA, (1973) 28 (1) 103-6.
 Journal code: 7609417. ISSN: 0033-3158.
 PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 197308
 ENTRY DATE: Entered STN: 19900310
 Last Updated on STN: 19900310
 Entered Medline: 19730831

CT Check Tags: Animal
 Conditioning (Psychology)
 Cycloheximide: PD, pharmacology
 Drug Antagonism
 Escape Reaction
 *Memory: DE, drug effects
 Proteins: BI, biosynthesis
 RNA: BI, biosynthesis
 Rats
 Time Factors
 *Uracil Nucleotides: PD, pharmacology
 RN 63231-63-0 (RNA); 66-81-9 (Cycloheximide)
 CN 0 (Proteins); 0 (Uracil Nucleotides)

L97 ANSWER 3 OF 24 MEDLINE on STN
 ACCESSION NUMBER: 97198255 MEDLINE
 DOCUMENT NUMBER: 97198255 PubMed ID: 9046309
 TITLE: Improvement of cognitive deficits and decreased cholinergic
 neuronal cell loss and apoptotic cell death following
 neurotrophin infusion after experimental traumatic brain
 injury.
 AUTHOR: Sinson G; Perri B R; Trojanowski J Q; Flamm E S; McIntosh T
 K
 CORPORATE SOURCE: Division of Neurosurgery, University of Pennsylvania School
 of Medicine, Philadelphia, USA.
 CONTRACT NUMBER: GM34690 (NIGMS)
 NS P01-08803 (NINDS)
 NS R01-26818 (NINDS)
 SOURCE: JOURNAL OF NEUROSURGERY, (1997 Mar) 86 (3) 511-8.
 Journal code: 0253357. ISSN: 0022-3085.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 199703
 ENTRY DATE: Entered STN: 19970407
 Last Updated on STN: 19980206
 Entered Medline: 19970324

AB This study explores the effects of infusion of nerve growth factor (NGF)
 on behavioral outcome and cell death in the septal region using the
 clinically relevant model of fluid-percussion brain injury in the rat.
 Animals were subjected to fluid-percussion brain injury and 24 hours later
 a miniosmotic pump was implanted to infuse NGF (12 animals) or vehicle (12
 animals) directly into the region of maximum injury for 2 weeks. Four
 weeks postinjury the animals were tested for cognitive function using a
 Morris Water Maze paradigm. Neurological motor function was evaluated
 over a 4-week postinjury period. The rats receiving NGF infusions had
 significantly higher memory scores than vehicle-treated animals.
 Examination of the cholinergic neurons in the medial septal region using
 choline acetyltransferase immunohistochemistry demonstrated significant
 cell loss after injury. Infusion of NGF significantly attenuated loss of
 these cholinergic neurons. A second group of animals was subjected to

*No trans for
 on bus*

fluid-percussion brain injury alone (23 rats) or injury followed by NGF infusion (18 rats). These animals were killed between 24 hours and 2 weeks postinjury and the septal region was examined for the presence of apoptotic cells using the terminal deoxynucleotidyl transferase-mediated biotinylated-deoxyuridinetriphosphate nick-end labeling technique. Apoptotic cells were identified as early as 24 hours postinjury; their numbers peaked at 4 and 7 days, and then declined by 14 days. The NGF-treated animals had some apoptotic cells; however, even at 7 days there were significantly fewer of these cells. No significant motor differences were observed between the NGF- and vehicle-treated groups. These data indicate that NGF administration beginning 24 hours after fluid-percussion brain injury has a beneficial effect on cognition and results in sparing of cholinergic septal neurons. These improvements persist after cessation of NGF administration. The beneficial effects of NGF may be related to its ability to attenuate traumatically induced apoptotic cell death.

CT Check Tags: Animal; Male; Support, U.S. Gov't, P.H.S.

Apoptosis: DE, drug effects

Behavior, Animal: DE, drug effects

*Brain Injuries: DT, drug therapy

Brain Injuries: PA, pathology

Cell Count

Cell Death: DE, drug effects

Choline O-Acetyltransferase: DU, diagnostic use

*Cholinergic Fibers: DE, drug effects

Cholinergic Fibers: PA, pathology

Cognition: DE, drug effects

*Cognition Disorders: DT, drug therapy

DNA Nucleotidylexotransferase: DU, diagnostic use

Deoxyuracil Nucleotides: DU, diagnostic use

Hippocampus: DE, drug effects

Hippocampus: IN, injuries

Hippocampus: PA, pathology

Infusion Pumps

Memory: DE, drug effects

Motor Neurons: DE, drug effects

Nerve Growth Factors: AD, administration & dosage

*Nerve Growth Factors: TU, therapeutic use

*Neurons: DE, drug effects

Neurons: PA, pathology

Parietal Lobe: DE, drug effects

Parietal Lobe: IN, injuries

Parietal Lobe: PA, pathology

Psychomotor Performance: DE, drug effects

Rats

Rats, Sprague-Dawley

Septal Nuclei: DE, drug effects

Septal Nuclei: IN, injuries

Septal Nuclei: PA, pathology

Time Factors

Vehicles

RN 1173-82-6 (deoxyuridine triphosphate)

CN 0 (Deoxyuracil Nucleotides); 0 (Nerve Growth Factors); 0 (Vehicles); EC 2.3.1.6 (Choline O-Acetyltransferase); EC 2.7.7.31 (DNA Nucleotidylexotransferase)

L97 ANSWER 4 OF 24 MEDLINE on STN

ACCESSION NUMBER: 74127786 MEDLINE

DOCUMENT NUMBER: 74127786 PubMed ID: 4817915

TITLE: Increase of guanosine incorporation into RNA of hippocampal neurons by application of uridine monophosphate during a learning experiment.

AUTHOR: ~~Rutrich H L; Pohle W; Matthies H~~

SOURCE: BRAIN RESEARCH, (1974 Mar 29) 69 (1) 49-55.

Journal code: 0045503. ISSN: 0006-8993.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 197405
 ENTRY DATE: Entered STN: 19900310
 Last Updated on STN: 19900310
 Entered Medline: 19740528

CT Check Tags: Animal
 Autoradiography
 Behavior, Animal: DE, drug effects
 Discrimination Learning: DE, drug effects
 *Guanosine: ME, metabolism
 *Hippocampus: DE, drug effects
 Hippocampus: ME, metabolism
 *Learning: DE, drug effects
 Memory, Short-Term: DE, drug effects
 *RNA: BI, biosynthesis
 Rats
 Tritium
 *Uracil Nucleotides: PD, pharmacology
 Visual Perception
 RN 10028-17-8 (Tritium); 118-00-3 (Guanosine); 63231-63-0 (RNA)
 CN 0 (Uracil Nucleotides)

L97 ANSWER 5 OF 24 MEDLINE on STN
 ACCESSION NUMBER: 72186704 MEDLINE
 DOCUMENT NUMBER: 72186704 PubMed ID: 5067531
 TITLE: [Effect of nucleotide-monophosphates on the acquisition and
 extinction of conditioned reactions].
 Die Wirkung von Nucleotid-Monophosphaten auf die
 Akquisition und Extinktion bedingter Reaktionen.
 AUTHOR: Ott T; Lossner B; Matthies H
 SOURCE: PSYCHOPHARMACOLOGIA, (1972) 23 (3) 261-71.
 Journal code: 7609417. ISSN: 0033-3158.
 GERMANY, WEST: Germany, Federal Republic of
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: German
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 197207
 ENTRY DATE: Entered STN: 19900310
 Last Updated on STN: 19900310
 Entered Medline: 19720725

CT Check Tags: Animal; Male
 Adenosine Monophosphate: PD, pharmacology
 Avoidance Learning: DE, drug effects
 Behavior, Animal
 Cerebral Ventricles
 Conditioning (Psychology)
 *Conditioning, Classical: DE, drug effects
 Cytosine Nucleotides: PD, pharmacology
 Discrimination Learning: DE, drug effects
 *Extinction (Psychology): DE, drug effects
 Guanine Nucleotides: PD, pharmacology
 Injections, Spinal
 Memory: DE, drug effects
 Neurons: ME, metabolism
 *Nucleotides: PD, pharmacology
 Proteins: BI, biosynthesis
 Pyrimidine Nucleotides: PD, pharmacology
 RNA: BI, biosynthesis
 Rats
 Rats, Inbred Strains
 Thymine Nucleotides: PD, pharmacology
 Uracil Nucleotides: PD, pharmacology
 RN 61-19-8 (Adenosine Monophosphate); 63231-63-0 (RNA)
 CN 0 (Cytosine Nucleotides); 0 (Guanine Nucleotides); 0 (Nucleotides); 0
 (Proteins); 0 (Pyrimidine Nucleotides); 0 (Thymine Nucleotides); 0 (Uracil
 Nucleotides)

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L97 ANSWER 6 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 2003186082 EMBASE

TITLE: Combined uridine and choline administration improves
cognitive deficits in spontaneously hypertensive
rats.AUTHOR: De Bruin N.M.W.J.; Kiliaan A.J.; De Wilde M.C.; Broersen
L.M.CORPORATE SOURCE: N.M.W.J. De Bruin, Johnson/Johnson Pharmaceutical R., CNS,
Building 10, Turnhoutse weg 30, Beerse B-2340, Netherlands.
ndebruin@prdbe.jnj.comSOURCE: Neurobiology of Learning and Memory, (2003) 80/1 (63-79).
Refs: 88

ISSN: 1074-7427 CODEN: NLMEFR

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Rationale. Hypertension is considered a risk factor for the development of cognitive disorders, because of its negative effects on cerebral vasculature and blood flow. Genetically induced hypertension in rats has been associated with a range of cognitive impairments. Therefore, spontaneously hypertensive rats (SHR) can potentially be used as a model for cognitive deficits in human subjects. Consecutively, it can be determined whether certain food components can improve cognition in these rats. Objective. The present study aimed to determine whether SHR display specific deficits in attention, learning, and memory function. Additionally, effects of chronic uridine and choline administration were studied. Methods. 5-7 months old SHR were compared with normotensive Wistar-Kyoto (WKY) and Sprague-Dawley (SD) rats. (a) The operant delayed non-matching-to-position (DNMTP) test was used to study short-term memory function. (b) The five-choice serial reaction time (5-CSRT) task was used to assess selective visual attention processes. (c) Finally, the Morris water maze (MWM) acquisition was used as a measure for spatial learning and mnemonic capabilities. Results. (1) SHR exhibited significantly impaired performance in the 5-CSRT test in comparison with the two other rat strains. Both the SHR and WKY showed deficits in spatial learning when compared with the SD rats. (2) Uridine and choline supplementation normalized performance of SHR in the 5-CSRT test. (3) In addition, uridine and choline treatment improved MWM acquisition in both WKY and SHR rats. Conclusion. The present results show that the SHR have a deficiency in visual selective attention and spatial learning. Therefore, the SHR may provide an interesting model in the screening of substances with therapeutic potential for treatment of cognitive disorders. A combination of uridine and choline administration improved selective attention and spatial learning in SHR. .COPYRGT. 2003 Elsevier Science (USA). All rights reserved.

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L97 ANSWER 7 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 1999141343 EMBASE

TITLE: Modulation of spontaneous and stimulation-evoked
transmitter release from rat sympathetic neurons by the
cognition enhancer linopirdine: Insights into its
mechanisms of action.

AUTHOR: Kristufek D.; Koth G.; Motejlek A.; Schwarz K.; Huck S.;

CORPORATE SOURCE: Boehm S.
 Dr. S. Boehm, Institute of Neuropharmacology, University of
 Vienna, Waehringerstrasse 13a, A-1090 Vienna, Austria
 SOURCE: Journal of Neurochemistry, (1999) 72/5 (2083-2091).
 Refs: 36
 ISSN: 0022-3042 CODEN: JONRA
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 008 Neurology and Neurosurgery
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB The mechanisms by which the cognition enhancer linopirdine may affect transmitter release were investigated in cultures of rat superior cervical ganglion neurons. Overflow of previously incorporated [3H]noradrenaline evoked by 10 .mu.M UTP or 0.1 .mu.M bradykinin was enhanced by linopirdine at .gtoreq.3 .mu.M, overflow evoked by 25 mM K+, 100 .mu.M nicotine, or 300 .mu.M ATP was enhanced by linopirdine at .gtoreq.10 .mu.M, and overflow due to 40 mM K+ or electrical field stimulation was not altered by linopirdine. Ba2+ (0.3 mM) augmented the same types of stimulation-evoked overflow to a similar extent as linopirdine. K+ (25 mM), nicotine (100 .mu.M), and ATP (300 .mu.M) triggered transmitter release in a partially tetrodotoxin-resistant manner, and the release-enhancing action of linopirdine was lost in the presence of tetrodotoxin (1 .mu.M). Linopirdine (10 .mu.M) raised spontaneous tritium outflow and reduced currents through muscarinic K+ (K(M)) channels with a similar time course. The secretagogue action of linopirdine was concentration- and Ca2+-dependent and abolished by tetrodotoxin (1 .mu.M) or Cd2+ (100 .mu.M). Linopirdine (10 .mu.M) added to the partial inhibition of K(M) channels by 1 or 3 mM Ba2+ but not to the complete inhibition by 10 mM Ba2+. Likewise, the secretagogue action of 1 and 3 mM, but not that of 10 mM, Ba2+ was enhanced by linopirdine. These results indicate that linopirdine facilitates and triggers transmitter release via blockade of K(M) channels and suggest that these K+ channels are located at neuronal somata rather than at presynaptic sites.

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CT Medical Descriptors:
 *neurotransmitter release
 *sympathetic nerve
 *cognition
 concentration response
 calcium transport
 potassium transport
 cellular distribution
 membrane electrophysiology
 drug mechanism
 nonhuman
 rat
 animal tissue
 animal cell
 newborn
 article
 priority journal
 Drug Descriptors:
 *linopirdine: PD, pharmacology
 tetrodotoxin
 tritium
 barium
 noradrenalin: EC, endogenous compound
 uridine diphosphate: PD, pharmacology
 bradykinin: PD, pharmacology

nicotine: PD, pharmacology
adenosine triphosphate: PD, pharmacology
RN (linopirdine) 105431-72-9; (tetrodotoxin) 4368-28-9, 4664-41-9; (tritium)
10028-17-8; (barium) 7440-39-3; (noradrenalin) 1407-84-7, 51-41-2; (
uridine diphosphate) 58-98-0; (bradykinin) 58-82-2,
5979-11-3; (nicotine) 54-11-5; (adenosine triphosphate) 15237-44-2,
56-65-5, 987-65-5
CO Sigma (United States); RBI

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L97 ANSWER 8 OF 24 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 97141555 EMBASE
DOCUMENT NUMBER: 1997141555
TITLE: Developments in purine and pyridimidine receptor-based
therapeutics.
AUTHOR: Spedding M.; Williams M.
CORPORATE SOURCE: Dr. M. Williams, Neurological/Urological Dis. Res., Abott
Laboratories, 100 Abbott Park, Abbott Park, IL 60064,
United States
SOURCE: Drug Development Research, (1996) 39/3-4 (436-441).
Refs: 54
ISSN: 0272-4391 CODEN: DDREDK
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 002 Physiology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Progress in the identification of novel P1 and P2 receptor ligands has
continued to lag behind the explosion in receptor cloning, especially in
the P2 area. Nonetheless, a number of novel chemical entities and natural
receptor ligands are continuing to advance in clinical trials or,
alternatively have become important new tools to study receptor function.
Compounds of note with activity at the P1 receptor family include NNC
21-0136 (A1 agonist; preclinical; stroke); SCH 59761 (nonselective P1
agonist; preclinical; cardiovascular disorders); the A1 antagonists,
KFM-19 (BIIP-20; phase II) and MDL 102,503 development (status unknown)
that may have therapeutic potential as cognition enhancers. KF
17837 and related A(2A)-antagonists such as KW 6002 represent potential
novel treatments for Parkinson's disease. SCH 58261 (A(2A) receptor
antagonist; preclinical) is a novel nonxanthine antagonist ligand. KW 3902
(phase II), FK- 453/FK 113453 (possibly discontinued) and CVT-124 (phase
I) are A1 receptor-selective xanthine-based antagonists that have
potential in the treatment of renal diseases. NNC 53-0055 (preclinical) is
the first of a new series of selective A3 receptor agonists that modulate
cytokine production. MRS 1067, MRS 1067, MRS 1097, MRS 1222, L-249, 313,
and L-268, 605 (all preclinical) represent new A3-receptor antagonists. GP
3269 (preclinical) is an adenosine kinase inhibitor with potential
efficacy in septic shock, stroke, and pain. ARL 67085 (phase II) is an ATP
bioisostere that is an antagonist of the P(2T) receptor that is the first
of new generation of antithrombotic agents; Systemic ATP has reached phase
II trials as a novel approach to metastasis regression. The pyrimidine
nucleotide, UTP (phase II) is being examined as P2Y2 receptor agonist for
the treatment of cystic fibrosis.

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on STN
 CT Medical Descriptors:
 *cardiovascular disease
 *central nervous system
 *cognition
 *kidney disease
 *metastasis
 *pain
 *parkinson disease
 *septic shock
 *stroke
 conference paper
 drug research
 human
 nonhuman
 receptor binding
 Drug Descriptors:
 *adenosine kinase inhibitor: AN, drug analysis
 *adenosine kinase inhibitor: CM, drug comparison
 *adenosine kinase inhibitor: DV, drug development
 *adenosine kinase inhibitor: PD, pharmacology
 *adenosine receptor: EC, endogenous compound
 *adenosine receptor stimulating agent: AN, drug analysis
 *adenosine receptor stimulating agent: CM, drug comparison
 *adenosine receptor stimulating agent: DV, drug development
 *adenosine receptor stimulating agent: PD, pharmacology
 *purine p2-receptor: EC, endogenous compound
 *uridine triphosphate: CM, drug comparison
 *uridine triphosphate: PD, pharmacology
 RN (uridine triphosphate) 63-39-8

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L97 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:656581 HCAPLUS

DOCUMENT NUMBER: 139:197370

TITLE: Preparation of aryl ureas containing pyridine, quinoline and isoquinoline N-oxide functionality as kinase inhibitors

INVENTOR(S): Dumas, Jacques; Scott, William J.; Riedl, Bernd

PATENT ASSIGNEE(S): Bayer Corporation, USA

SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

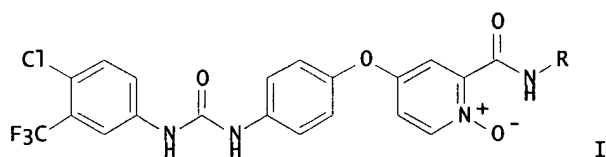
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068229	A1	20030821	WO 2003-US4110	20030211
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2002-354935P P 20020211

OTHER SOURCE(S): MARPAT 139:197370

GI



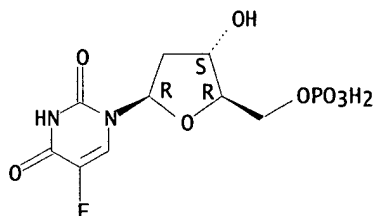
AB The title ureas contg. a pyridine, quinoline, or isoquinoline functionality which is oxidized at the nitrogen heteroatom MLBNHCONHA [A = (un)substituted Ph, naphthyl, 5-6 membered monocyclic heteroaryl, 8-10 membered bicyclic heteroaryl; B = (un)substituted phenylene, naphthylene, 5-6 membered monocyclic heteroarylene, 8-10 membered bicyclic heteroarylene; L = (CH₂)_mO(CH₂)_l, (CH₂)_m(CH₂)_l, (CH₂)_mCO(CH₂)_l, etc.; m, l = 0-4; M = (un)substituted pyridine-1-oxide, quinoline-1-oxide, isoquinoline-1-oxide; with the provisos] which are useful in the treatment of (i) raf mediated diseases, for example, cancer, (ii) p38 mediated diseases such as inflammation and osteoporosis, and (iii) VEGF mediated diseases such as angiogenesis disorders, were claimed. Prepn. of two ureas such as I [R = H, Me] which are not compds. of the invention, and have been distinguished from the compds. of the invention by a proviso, was described. Pharmaceutical compn. comprising the title ureas was claimed.

IT 134-46-3, 5-Fluorodeoxyuridine monophosphate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of aryl ureas contg. pyridine, quinoline and isoquinoline
N-oxide functionality for use in combination with other
anti-proliferative agent)

RN 134-46-3 HCAPLUS

CN 5'-Uridylic acid, 2'-deoxy-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L97 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:315467 HCAPLUS

DOCUMENT NUMBER: 136:335248

TITLE: Pyrimidine nucleotide precursors for the treatment of mitochondrial diseases

INVENTOR(S): Von Borstel, Reid W.; Saydoff, Joel A.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U. S. Ser. No. 763,955.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002049182	A1	20020425	US 2001-930494	20010816
US 2001005719	A1	20010628	US 1998-144096	19980831
US 6472378	B2	20021029		
WO 2000011952	A1	20000309	WO 1999-US19725	19990831
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
WO 2003015516	A1	20030227	WO 2002-US25831	20020814
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

US 1998-144096 A2 19980831
 WO 1999-US19725 W 19990831
 US 2001-763955 A2 20010228
 US 2001-930494 A 20010816

AB Compds., compns., and methods are provided for the treatment of disorders related to mitochondrial dysfunction. The methods comprise administering to a mammal a compn. contg. pyrimidine nucleotide precursors in amts. sufficient to treat symptoms resulting from mitochondrial respiratory chain deficiencies.

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L97 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

IC ICM A61K048-00

NCL 514044000

CC 1-10 (Pharmacology)

Section cross-reference(s): 33, 63

ST pyrimidine nucleotide precursor therapeutic mitochondrial respiratory chain deficiency; mitochondrial dysfunction treatment pyrimidine nucleotide precursor

IT Nervous system, disease

(Friedreich's ataxia; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Nervous system, disease

(Huntington's chorea; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Muscle, disease

(Keams-Sayres Syndrome; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Brain, disease

(Leigh's disease; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Brain, disease

(MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes); pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Muscle, disease

(MERRF (myoclonic epilepsy assocd. with ragged-red muscle fibers); pyrimidine nucleotide precursors for the treatment of mitochondrial

- diseases)
- IT Disease, animal
(NARP (neurogenic muscle weakness, ataxia, and retinitis pigmentosa);;
pyrimidine nucleotide precursors for the treatment of mitochondrial
diseases)
- IT Eye, disease
(PEO (chronic progressive external ophthalmoplegia); pyrimidine
nucleotide precursors for the treatment of mitochondrial diseases)
- IT Brain, disease
(Rett's Syndrome; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Cognition
(age-related decline in; pyrimidine nucleotide precursors for the
treatment of mitochondrial diseases)
- IT Nervous system, disease
(ataxia; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Mental disorder
(attention deficit hyperactivity disorder; pyrimidine nucleotide
precursors for the treatment of mitochondrial diseases)
- IT Mental disorder
(autism; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Nervous system, disease
(autonomic neuropathy; pyrimidine nucleotide precursors for the
treatment of mitochondrial diseases)
- IT Heart, disease
(cardiomyopathy, dilating; pyrimidine nucleotide precursors for the
treatment of mitochondrial diseases)
- IT Muscle
(cells; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Fatigue, biological
(chemotherapy-assocd.; pyrimidine nucleotide precursors for the
treatment of mitochondrial diseases)
- IT Menopause
(chemotherapy-induced; pyrimidine nucleotide precursors for the
treatment of mitochondrial diseases)
- IT Fatigue, biological
(chronic fatigue syndrome; pyrimidine nucleotide precursors for the
treatment of mitochondrial diseases)
- IT Brain
(corpus striatum; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(defective nuclear-encoded, components of the mitochondrial respiratory
chain; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Nervous system, disease
(degeneration; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Mutation
(deletion; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Appetite
(depressed; pyrimidine nucleotide precursors for the treatment of
mitochondrial diseases)
- IT Mitochondria
(disease, congenital; pyrimidine nucleotide precursors for the
treatment of mitochondrial diseases)
- IT Mitochondria
(disease, mitochondrial respiratory chain deficiency; pyrimidine
nucleotide precursors for the treatment of mitochondrial diseases)
- IT Development, mammalian postnatal
(disorder, developmental delay in cognitive, motor, language, executive
function, or social skills; pyrimidine nucleotide precursors for the

- treatment of mitochondrial diseases)
- IT Liver, disease
(failure; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Eye, disease
(hereditary optic atrophy; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Acidosis
(lactic; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Behavior
(locomotor; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Headache
(migraine; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Respiration, animal
(mitochondrial, dysfunction, respiratory chain deficiency; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Heart
(myocyte; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Muscular dystrophy
(myotonic; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Bladder, disease
Intestine, disease
(neurogenic, dysfunction; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Nerve
(neuron; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Cell death
(neuronal; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Nerve, disease
(neuropathy, MNGIE (myopathy neuropathy gastrointestinal dysmotility encephalopathy); pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Nerve, disease
(neuropathy, optic nerve (eye); pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Cytoprotective agents
(neuroprotectants; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Toxins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(neurotoxins; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Hepatitis
(nonalc. steatohepatitis; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Drug delivery systems
(oral; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Nerve, disease
Nerve, disease
(peripheral neuropathy; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Cell
(post-mitotic; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)
- IT Aging, animal
Alzheimer's disease
Anti-Alzheimer's agents
Anticonvulsants

Antimigraine agents
 Antiparkinsonian agents
 Antitumor agents
 Antitumor agents
 Behavior
 Cell death
 Chemotherapy
 Cognition enhancers
 Cytoprotective agents
 Death
 Disease models
 Drug interactions
 Epilepsy
 Muscular dystrophy
 Mutation
 Nervous system agents
 Neuromuscular diseases
 Parkinson's disease
 Statistical analysis

(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Mitochondrial DNA

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Pyrimidine nucleosides

Pyrimidine nucleotides

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Mitochondrial DNA

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (rearrangement of; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Acidosis

(renal tubular; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Deafness

(sensorineural; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT Kidney, disease

(tubular acidosis; pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 33069-62-4, Taxol

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
 (pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 51-61-6, Dopamine, biological studies 57-00-1, Creatine 9000-83-3, Complex V (Mitochondrial electron transport) 9001-16-5, Mitochondrial electron transport complex IV 9027-03-6, Mitochondrial electron transport complex III 9028-04-0, Mitochondrial electron transport complex I 9028-11-9, Mitochondrial electron transport complex II
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 127-17-3, Pyruvic acid, biological studies

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 58-96-8DP, Uridine, acyl deriv. 65-46-3DP, Cytidine, acyl deriv. 260360-01-8P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

IT 58-96-8, Uridine 65-46-3, Cytidine 65-86-1, Orotic acid 65-86-1D, Orotic acid, esters 127-17-3D, Pyruvic acid, esters 303-98-0, Coenzyme Q10 987-78-0, Cytidine diphosphocholine 1747-53-1, Ethyl orotate 4105-38-8, 2',3',5'-Tri-O-acetyluridine 260360-02-9 260360-03-0 260360-04-1 260360-05-2 260360-06-3 260360-07-4
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine nucleotide precursors for the treatment of mitochondrial diseases)

=> d ibib abs hitstr 11

L97 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:208065 HCAPLUS
DOCUMENT NUMBER: 134:242656
TITLE: Phospholipid prodrugs of anti-proliferative drugs
INVENTOR(S): Kozak, Alexander; Shapiro, Israel; Vinnikova, Marina; Ershov, Leonid; Senderikhin, Alexander; Ayalon, Oran
PATENT ASSIGNEE(S): D-Pharm Limited, Israel
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019320	A2	20010322	WO 2000-IL562	20000913
WO 2001019320	A3	20010927		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2000073093	A5	20010417	AU 2000-73093	20000913
EP 1218013	A2	20020703	EP 2000-960946	20000913
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
JP 2003514770	T2	20030422	JP 2001-522958	20000913
NZ 517522	A	20030829	NZ 2000-517522	20000913
ZA 2002001081	A	20030207	ZA 2002-1081	20020207
PRIORITY APPLN. INFO.:			IL 1999-131887 A	19990914
			WO 2000-IL562 W	20000913

OTHER SOURCE(S): MARPAT 134:242656

AB The invention discloses prodrugs comprising anti-proliferative drugs covalently linked, via a bridging group, to a phospholipid moiety such that the active species is preferentially released, preferably by enzymic cleavage, at the required site of action. The invention further discloses pharmaceutical compns. comprising said prodrugs and the uses thereof for the treatment of diseases and disorders related to inflammatory, to degenerative or atrophic conditions, and to uncontrolled cell growth. A methotrexate deriv. 1-stearoyl-2-[3-(.alpha.-dodecylate-.gamma.-methotrexate-amido)-propanoyl]-sn-glycero-3-phosphatidylcholine was prepd., and examd. for its inhibitory effect on human leukemia cell growth.

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L97 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
 IC ICM A61K
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1
 ST cell growth inhibitor phospholipid deriv prepn; methotrexate antitumor
 phospholipid deriv prodrug prepn
 IT Antitumor agents
 (Burkitt's lymphoma; phospholipid prodrugs of anti-proliferative drugs)
 IT Nervous system
 (Huntington's chorea, treatment of; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Mental disorder
 (Pick's disease, treatment of; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Drug delivery systems
 (aerosols; phospholipid prodrugs of anti-proliferative drugs)
 IT Nervous system
 (amyotrophic lateral sclerosis, treatment of; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Antitumor agents
 (bladder; phospholipid prodrugs of anti-proliferative drugs)
 IT Drug delivery systems
 (capsules; phospholipid prodrugs of anti-proliferative drugs)
 IT Brain, disease
 (cerebrovascular, treatment of; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Uterus, neoplasm
 (cervix, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
 IT Antitumor agents
 (cervix; phospholipid prodrugs of anti-proliferative drugs)
 IT Chorion
 (choriocarcinoma, inhibitors; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Antitumor agents
 (choriocarcinoma; phospholipid prodrugs of anti-proliferative drugs)
 IT Intestine, neoplasm
 (colon, inhibitors; phospholipid prodrugs of anti-proliferative drugs)
 IT Antitumor agents
 (colon; phospholipid prodrugs of anti-proliferative drugs)
 IT Nervous system
 (degeneration, treatment of; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Mental disorder
 (dementia, multi-infarct, treatment of; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Mental disorder
 (dementia, treatment of; phospholipid prodrugs of anti-proliferative
 drugs)
 IT Mental disorder
 (dementia, vascular, treatment of; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Nerve, disease
 (diabetic neuropathy, treatment of; phospholipid prodrugs of
 anti-proliferative drugs)
 IT Nervous system
 (disease, treatment of; phospholipid prodrugs of anti-proliferative
 drugs)
 IT Mycosis
 (fungoides, inhibitors; phospholipid prodrugs of anti-proliferative
 drugs)
 IT Drug delivery systems
 (gels; phospholipid prodrugs of anti-proliferative drugs)
 IT Antitumor agents
 (head; phospholipid prodrugs of anti-proliferative drugs)
 IT Liver, neoplasm

(hepatoma, inhibitors; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(hepatoma; phospholipid prodrugs of anti-proliferative drugs)

IT Neoplasm
(hydatidiform mole, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Intestine, disease
(inflammatory bowel syndromes, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Intestine, neoplasm
Lung, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Skin, neoplasm
(inhibitors; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(injections, i.v.; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(intestine; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(lung; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(lymphocytic leukemia; phospholipid prodrugs of anti-proliferative drugs)

IT Eye, disease
(macula, degeneration, age-related, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(mammary gland; phospholipid prodrugs of anti-proliferative drugs)

IT Headache
(migraine, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Skin, neoplasm
(mycosis fungoides, inhibitors; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(mycosis fungoides; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(myelogenous leukemia; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(nasal; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(neck; phospholipid prodrugs of anti-proliferative drugs)

IT Bladder
Head
Mammary gland
Neck, anatomical
Prostate gland
Urinary tract
(neoplasm, inhibitors; phospholipid prodrugs of anti-proliferative drugs)

IT Trophoblast
(neoplasm, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(non-Hodgkin's lymphoma; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(ointments; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(ophthalmic; phospholipid prodrugs of anti-proliferative drugs)

IT Nerve
(optic, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems

(oral; phospholipid prodrugs of anti-proliferative drugs)

IT Pharynx
(oropharynx carcinoma, inhibitors; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(oropharynx carcinoma; phospholipid prodrugs of anti-proliferative drugs)

IT Bone, neoplasm
(osteosarcoma, inhibitors; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(osteosarcoma; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(ovary; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(pancreas; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(parenterals; phospholipid prodrugs of anti-proliferative drugs)

IT Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antiparkinsonian agents
Antirheumatic agents
Antitumor agents
(phospholipid prodrugs of anti-proliferative drugs)

IT Lysophosphatidylcholines
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(prodrugs; phospholipid prodrugs of anti-proliferative drugs)

IT Proliferation inhibition
(proliferation inhibitors; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(prostate gland; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(rectal; phospholipid prodrugs of anti-proliferative drugs)

IT Connective tissue
(scleroderma, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(skin; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(solns.; phospholipid prodrugs of anti-proliferative drugs)

IT Brain, disease
(stroke, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(suppositories; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(suspensions; phospholipid prodrugs of anti-proliferative drugs)

IT Lupus erythematosus
(systemic, treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(tablets; phospholipid prodrugs of anti-proliferative drugs)

IT Drug delivery systems
(topical; phospholipid prodrugs of anti-proliferative drugs)

IT Granulomatous disease
Multiple sclerosis
Psoriasis
(treatment of; phospholipid prodrugs of anti-proliferative drugs)

IT Antitumor agents
(urinary tract; phospholipid prodrugs of anti-proliferative drugs)

IT 9001-84-7, Phospholipase A2 9013-93-8, Phospholipase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(activated by; phospholipid prodrugs of anti-proliferative drugs)
 IT 330658-48-5P 330658-49-6P 330658-50-9P 330658-51-0P 330658-52-1P
 330658-55-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of phospholipid prodrugs of anti-proliferative drugs)
 IT 330658-53-2 330658-54-3
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (prepn. of phospholipid prodrugs of anti-proliferative drugs)
 IT 50-91-9, 5-Fluoro-2'-deoxyuridine 56-12-2, 4-Aminobutanoic acid, reactions 59-05-2, Methotrexate 60-32-2, 6-Aminohexanoic acid 64-19-7, Acetic acid, reactions 76-83-5, Trityl chloride 107-95-9, 3-Aminopropanoic acid 123-76-2, Levulinic acid 501-53-1, Benzyl chloroformate 660-88-8, 5-Aminovaleric acid 1002-57-9, 8-Aminooctanoic acid 1069-66-5, Sodium 2-Propylpentanoate 4160-82-1, 3,3-Dimethylglutaric anhydride 19420-57-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (prepn. of phospholipid prodrugs of anti-proliferative drugs)
 IT 1947-00-8P, 6-[N-(Benzyloxycarbonyl)amino]hexanoic acid 2304-94-1P
 5066-71-7P 5105-78-2P 10343-71-2P 23135-50-4P 23434-40-4P
 57444-77-6P 76523-73-4P 93349-30-5P 112489-84-6P 163225-49-8P
 271781-53-4P 330658-56-5P 330658-57-6P 330658-58-7P 330658-59-8P
 330658-60-1P 330658-62-3P 330658-64-5P 330658-66-7P 330658-68-9P
 330658-69-0P 330658-70-3P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of phospholipid prodrugs of anti-proliferative drugs)

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L97 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:703740 HCAPLUS

DOCUMENT NUMBER: 135:251986

TITLE: Methods for treating fibroproliferative diseases with antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides

INVENTOR(S): Peterson, Theresa C.

PATENT ASSIGNEE(S): Dalhousie University, Can.

SOURCE: U.S., 13 pp., Cont.-in-part of U.S. 6,025,151.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6294350	B1	20010925	US 1999-433621	19991102
US 5985592	A	19991116	US 1997-870096	19970605
US 6025151	A	20000215	US 1998-92317	19980605
WO 2001032156	A2	20010510	WO 2000-IB1731	20001102
WO 2001032156	A3	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1997-870096 A2 19970605
 US 1998-92317 A2 19980605

US 1999-433621 A1 19991102

AB In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization of c-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence of Jun kinase are treated by administering to the subject an amt. of a compd. effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxifylline, or a functional deriv. or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compd. is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L97 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
 IC ICM C12Q001-02
 ICS C12Q001-00; C12Q001-50
 NCL 435029000
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 9, 63
 ST fibroproliferative disease treatment antiproliferative antifibrotic agent;
 antiproliferative antisense oligonucleotide fibroproliferative disease
 cJun
 IT Peptides, biological studies
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
 BSU (Biological study, unclassified); BIOL (Biological study); PROC
 (Process)
 (ATF2; antiproliferative or antifibrotic agents, esp. antisense c-Jun
 oligonucleotides, for treating fibroproliferative diseases)
 IT Angiotensin receptors
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (AT1, inhibitors; antiproliferative or antifibrotic agents, esp.
 antisense c-Jun oligonucleotides, for treating fibroproliferative
 diseases)
 IT Hepatitis
 (C; antiproliferative or antifibrotic agents, esp. antisense c-Jun
 oligonucleotides, for treating fibroproliferative diseases)
 IT Transcription factors
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
 effector, except adverse); BPR (Biological process); BSU (Biological
 study, unclassified); BIOL (Biological study); PROC (Process)
 (CREB (cAMP-responsive element-binding); antiproliferative or
 antifibrotic agents, esp. antisense c-Jun oligonucleotides, for
 treating fibroproliferative diseases)
 IT Eye, disease
 Graves' disease
 (Graves' ophthalmopathy; antiproliferative or antifibrotic agents, esp.
 antisense c-Jun oligonucleotides, for treating fibroproliferative
 diseases)
 IT Sarcoma
 (Kaposi's; antiproliferative or antifibrotic agents, esp. antisense
 c-Jun oligonucleotides, for treating fibroproliferative diseases)
 IT Neoplasm
 (Li-Fraumeni syndrome; antiproliferative or antifibrotic agents, esp.
 antisense c-Jun oligonucleotides, for treating fibroproliferative
 diseases)
 IT Transcription factors
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);

- BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence) (NF-.kappa.B (nuclear factor .kappa.B); antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Peptides, biological studies
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (Nrfl; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Eye
 (Tenon's capsule, fibroproliferation; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Leukemia
 (acute myelogenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Abdomen
 (adhesions; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Fibrosis
 (antifibrotics; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Alzheimer's disease
 Animal tissue culture
 Anti-Alzheimer's agents
 Antitumor agents
 Drug screening
 Epithelium
 Fibroblast
 Hematopoietic precursor cell
 Keloid
 Kidney, disease
 Leprosy
 Mesenchyme
 Multiple sclerosis
 Myelodysplastic syndromes
 Myeloproliferative disorders
 Neoplasm
 Neuroglia
 Phosphorylation, biological
 Picrorhiza kurroa
 Signal transduction, biological
 Silicosis
 Silybum marianum.
 Test kits
 (antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Platelet-derived growth factors
 Tumor necrosis factors
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
 (antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Antisense oligonucleotides
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Decorins
 Phosphatidylcholines, biological studies
 Tocopherols

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Bronchi

(bronchiolitis, obliterative; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Signal peptides

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(c-Jun heterodimerization with; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Transcription factors

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process)

(c-jun; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Malaria

(cerebral; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Intestine, disease

(colitis, collagenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Cardiovascular system

(disease; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drugs

Ergot (Claviceps)

(drug-induced ergotism; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Reproductive tract

(female, cancer; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Intestine

Lung

Skin

(fibroblasts of; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Radiation

(fibrosis from; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Heart, disease

Kidney, disease

Liver, disease

Lung, disease

Peritoneum

(fibrosis; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Gene, animal

RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)

(for c-Jun; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Neuroglia

- (glioblastoma, sporadic; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Neuroglia
(glioblastoma; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Kidney, disease
(glomerulonephritis; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Neutrophil
(infiltration; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Intestine, disease
(inflammatory; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Cytokines
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(inflammatory; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Drug delivery systems
(inhalants; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Drug delivery systems
(injections, i.m.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Drug delivery systems
(injections, i.v.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Lung, disease
(interstitial; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Brain, disease
(malaria; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Antitumor agents
(mammary gland; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Kidney
(mesangium; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Leukemia
(myelogenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Liver
(myofibroblasts of; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Mammary gland
(neoplasm, inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Mammary gland
(neoplasm; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Nerve, neoplasm
(neuroblastoma; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Drug delivery systems
(oral; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

- IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence) (p65, NF-.kappa.B p65; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT **Phosphatidylcholines, biological studies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polyenyl-; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Proliferation inhibition
(proliferation inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Disease, animal
(proliferative; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Drug delivery systems
(rectal; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Connective tissue
(scleroderma; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Shock (circulatory collapse)
(septic; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Blood vessel
(smooth muscle; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Muscle
(smooth; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Carcinoma
(squamous cell, differentiation disorder; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Cell differentiation
(squamous cell, disorder; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Drug delivery systems
(sustained-release; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Lupus erythematosus
(systemic, nephritis assocd. with; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Drug delivery systems
(topical; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Drug delivery systems
(transdermal; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Interferons
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (.alpha.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.-, RII/FC; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

- IT 155215-87-5, Jun kinase
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT 217308-10-6, DNA, d(G-C-A-G-T-C-A-T-A-G-A-A-C-A-G-T-C-C-G-T-C-A-C-T-T-C-A-C-G-T)
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT 50-23-7, Hydrocortisone 54-85-3, Isoniazid 54-85-3D, Isoniazid, conjugated 59-67-6, Niacin, biological studies 64-86-8, Colchicine 107-35-7, Taurine 518-34-3, Tetrandrine 1028-33-7, Pentifylline 1405-86-3, Glycyrrhizin 6493-05-6, Pentoxifylline 6493-05-6D, Pentoxifylline, derivs. and metabolites 6493-06-7, 1H-Purine-2,6-dione, 3,7-dihydro-1-(5-hydroxyhexyl)-3,7-dimethyl- 10102-43-9, Nitric oxide, biological studies 53179-13-8, Pirfenidone 55242-55-2, Propentofylline 55837-20-2, Halofuginone 62571-86-2, Captopril 75847-73-3, Enalapril 80288-49-9, Furafllyline 83150-76-9, Octreotide 85721-33-1, Ciprofloxacin 91161-71-6, Terbinafine 114798-26-4, Losartan 119290-87-8, Acanthoic acid 120210-48-2, Tenidap
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT 50-88-4, Tritiated thymidine, biological studies 1148-63-6, Thymidine-.alpha.-t 42459-79-0, Uridine, 5-bromo-, labeled with tritium
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT 330196-64-0, Cytochrome p 450 1A2
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
- IT 9015-82-1, Angiotensin converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

=> d ibib abs hitstr 13

L97 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:624138 HCAPLUS

DOCUMENT NUMBER: 135:175416

TITLE: Uridylic acid, guanylic acid, uridine and/or guanosine for improving learning and memory functions

INVENTOR(S): Azehiru, Toichi; Endo, Kazuki; Miyazaki, Shuichi

PATENT ASSIGNEE(S): Yamasa Shoyu Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001233776	A2	20010828	JP 2000-48714	20000225

PRIORITY APPLN. INFO.: JP 2000-48714 20000225

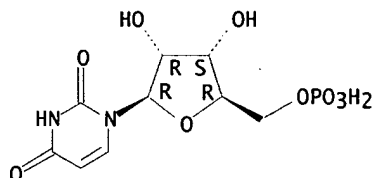
AB Uridylic acid, guanylic acid, uridine and/or guanosine are claimed as health foods for improving learning and memory functions esp. for Alzheimer's disease. The learning- and memory-enhancing effects were tested in aged rats.

IT 58-97-9, Uridylic acid, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (uridylic acid, guanylic acid, uridine and/or guanosine for improving learning and memory functions)

RN 58-97-9 HCAPLUS

CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr 14

L97 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:608584 HCAPLUS

DOCUMENT NUMBER: 133:187987

TITLE: Methods using pyrimidine-based nucleosides for treatment of mitochondrial disorders

INVENTOR(S): Naviaux, Robert K.

PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: PCT Int. Appl., 28 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050043	A1	20000831	WO 2000-US4663	20000223

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

NZ 513926 A 20010928 NZ 2000-513926 20000223

BR 2000008447 A 20020115 BR 2000-8447 20000223

EP 1171137 A1 20020116 EP 2000-910321 20000223

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2002537340 T2 20021105 JP 2000-600654 20000223
 PRIORITY APPLN. INFO.: US 1999-121588P P 19990223
 WO 2000-US4663 W 20000223

OTHER SOURCE(S): MARPAT 133:187987

AB Methods are provided for the treatment of mitochondrial disorders. The methods include the administration of a pyrimidine-based nucleoside, e.g. **triacetyluridine**. Also provided are methods of reducing or eliminating symptoms assocd. with mitochondrial disorders. Mitochondrial disorders particularly appropriate for treatment include those attributable to a deficiency of one or more pyrimidines.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 14

L97 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

IC ICM A61K031-70

CC 1-12 (Pharmacology)

ST pyrimidine nucleoside deriv mitochondrial disorder treatment;
triacetyluridine mitochondrial disorder treatment

IT Transport proteins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(ADP/ATP carrier, deficiency; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Disease, animal

(Alpers syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Disease, animal

(Asperger syndrome with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Nervous system

(Huntington's chorea; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Muscle, disease

(Kearns-Sayre syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Brain, disease

(Leigh's disease; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Disease, animal

(MARIAHS; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Brain, disease

(MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes); pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Muscle, disease

(MERRF (myoclonic epilepsy assocd. with ragged-red muscle fibers); pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Disease, animal

(MNGIE; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Disease, animal

(NARP/MILS; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Bone marrow, disease

Pancreas, disease

(Pearson marrow-pancreas syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Disease, animal

(Wolfram syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT Antibiotics

(aminoglycoside, deafness assocd. with; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

- IT Deafness
(aminoglycoside-assocd.; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Nervous system
(amyotrophic lateral sclerosis; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Vitamins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and cofactors; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Mental disorder
(attention deficit hyperactivity disorder; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Mental disorder
(autism, autism with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Carboxylic acids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(carboxylic aciduria, ethylmalonic aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Heart, disease
(cardiomyopathy; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Movement disorders
(cerebral palsy, with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Eye, disease
(chronic progressive external ophthalmoplegia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Antiemetics
(cyclic vomiting syndrome with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Cardiolipins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(deficiency; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Mental disorder
(dementia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Antidiabetic agents
(diabetes mellitus lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Carboxylic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dicarboxylic, pyrimidine nucleoside derivs.; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Heart, disease
(dilated cardiomyopathy; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Mitochondria
(diseases; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Learning
(disorder, dyslexia, with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Toxicity
(drug; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Nervous system
(dystonia, ND6; pyrimidine-based nucleoside for treatment of mitochondrial disorder)

- IT Necrosis
(familial bilateral striatal; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Eye, disease
(hereditary optic atrophy; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Eye, disease
(impaired eyesight; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Acidosis
(lactic, ethylmalonic aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Antitumor agents
(leukemia, thrombocytopenia and leukemia syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Spleen, neoplasm
Spleen, neoplasm
(lymphoma, inhibitors; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Disease, animal
(mtDNA depletion syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Disease, animal
(multiple mtDNA deletion syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nuclear; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Enzymes, biological studies
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(of pyrimidine synthetic pathway; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Amino acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine nucleoside derivs.; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Pyrimidine bases
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(pyrimidine synthetic pathway; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Anticonvulsants
Cardiovascular agents
Mutation
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Pyrimidine nucleosides
Ubiquinones
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Mitochondrial DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Infection
(refractory epilepsy or Asperger syndrome or autism with declines during infection; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Acidosis

- (renal tubular; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Muscle, disease
(skeletal and peripheral and autonomic; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Antitumor agents
(spleen lymphoma; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Platelet (blood)
(thrombocytopenia, thrombocytopenia and leukemia syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Kidney, disease
(tubular acidosis; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT Nervous system agents
(uridine-responsive neurol. syndrome; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 300-85-6, 3-Hydroxybutyric acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(3-hydroxybutyric aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 5746-90-7, 3-Methylglutaconic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(3-methylglutaconic aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 9000-83-3, Complex V (mitochondrial electron transport) 9001-16-5, Complex IV (mitochondrial electron transport) 9002-02-2, Succinate dehydrogenase 9014-20-4, Pyruvate dehydrogenase 9027-03-6, Complex III (mitochondrial electron transport) 9028-04-0, Complex I (mitochondrial electron transport) 9028-11-9, Complex II (mitochondrial electron transport)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(deficiency; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 601-75-2, Ethylmalonic acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ethylmalonic aciduria with lactic acidemia; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 51-35-4, Hydroxyproline
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(hydroxyprolinuria; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 9001-92-7, Protease 9068-38-6, Reverse transcriptase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 3056-17-5, Stavudine 7481-89-2, Zalcitabine 30516-87-1, Azidothymidine 69123-98-4, FIAU 69655-05-6, Didanosine 75706-12-6, Leflunomide 96187-53-0, Brequinar 127779-20-8, Saquinavir 150378-17-9, Indinavir 155213-67-5, Ritonavir 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 9029-03-2, Dihydroorotate dehydrogenase 74870-74-9, Uridine monophosphate synthase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pyrimidine-based nucleoside for treatment of mitochondrial disorder)
- IT 51-35-4D, L-Hydroxyproline, pyrimidine nucleoside derivs. 52-90-4D, L-Cysteine, pyrimidine nucleoside derivs., biological studies 56-40-6D, Glycine, pyrimidine nucleoside derivs., biological studies 56-41-7D, L-Alanine, pyrimidine nucleoside derivs., biological studies 56-45-1D,

L-Serine, pyrimidine nucleoside derivs., biological studies 56-84-8D,
 L-Aspartic acid, pyrimidine nucleoside derivs., biological studies
 56-86-0D, L-Glutamic acid, pyrimidine nucleoside derivs., biological
 studies 56-87-1D, L-Lysine, pyrimidine nucleoside derivs., biological
 studies 56-89-3D, L-Cystine, pyrimidine nucleoside derivs., biological
 studies 58-85-5, Biotin 59-30-3, Folic acid, biological studies
 59-43-8, Vitamin B1, biological studies 59-67-6, Niacin, biological
 studies 60-18-4D, L-Tyrosine, pyrimidine nucleoside derivs., biological
 studies 61-90-5D, L-Leucine, pyrimidine nucleoside derivs., biological
 studies 68-19-9, Vitamin B12 70-26-8D, L-Ornithine, pyrimidine
 nucleoside derivs. 71-00-1D, L-Histidine, pyrimidine nucleoside derivs.,
 biological studies 72-18-4D, L-Valine, pyrimidine nucleoside derivs.,
 biological studies 72-19-5D, L-Threonine, pyrimidine nucleoside derivs.,
 biological studies 73-32-5D, L-Isoleucine, pyrimidine nucleoside
 derivs., biological studies 74-79-3D, L-Arginine, pyrimidine nucleoside
 derivs., biological studies 79-83-4, Pantothenic acid 83-88-5, Vitamin
 B2, biological studies 147-85-3D, L-Proline, pyrimidine nucleoside
 derivs., biological studies 541-15-1D, L-Carnitine, pyrimidine
 nucleoside derivs. 4105-38-8 8059-24-3, Vitamin B6 52009-14-0,
 Calcium pyruvate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)

(pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT 71-52-3, Bicarbonate, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(pyrimidine-based nucleoside for treatment of mitochondrial disorder)

IT 58-96-8, Uridine

RL: BPR (Biological process); BSU (Biological study, unclassified); MFM
 (Metabolic formation); BIOL (Biological study); FORM (Formation,
 nonpreparative); PROC (Process)

(pyrimidine-based nucleoside for treatment of mitochondrial disorder)

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L97 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:98343 HCAPLUS

DOCUMENT NUMBER: 132:132349

TITLE: Methods using uridine or a uridine
 source for increasing cytidine levels in vivo and
 treating cytidine-dependent human neurological
 diseases

INVENTOR(S): Watkins, Carol; Wurtman, Richard J.

PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA

SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

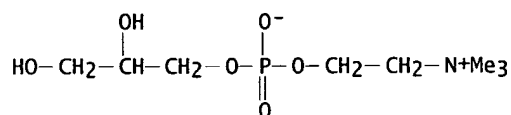
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006174	A1	20000210	WO 1999-US17235	19990730
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2339008	AA	20000210	CA 1999-2339008	19990730
EP 1140104	A1	20011010	EP 1999-937631	19990730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE, MC, PT, IE, FI				
US 2002028787	A1	20020307	US 1999-363748	19990730
JP 2003517437	T2	20030527	JP 2000-562028	19990730
PRIORITY APPLN. INFO.: US 1998-95002P P 19980731				
WO 1999-US17235 W 19990730				

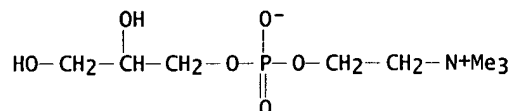
AB Methods of treating certain neurol. diseases using exogenous **uridine** or a **uridine** source alone as a precursor of endogenous cytidine, particularly in the human brain, are disclosed. Methods are also disclosed in which exogenous **uridine** or a **uridine** source is combined either with drugs increasing **uridine** availability or with compds. that serve as a source of choline in phospholipid synthesis.

IT 563-24-6, Glycerophosphatidylcholine 563-24-6D, Glycerophosphocholine, acyl derivs.
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (uridine or uridine source for increasing cytidine levels in vivo and treating cytidine-dependent human neurol. diseases)

RN 563-24-6 HCAPLUS
 CN Ethanaminium, 2-[[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)



RN 563-24-6 HCAPLUS
 CN Ethanaminium, 2-[[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 16

L97 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:798788 HCAPLUS

DOCUMENT NUMBER: 130:148627

TITLE: Effects of nucleotides on learning and memory in a morris water maze test in normal and basal forebrain-lesioned rats

AUTHOR(S): Miyazaki, Shuichi; Imaizumi, Masahiro; Abiru, Toichi; Machida, Haruhiko

CORPORATE SOURCE: Biology Laboratory, Yamasa Corporation, Chiba, 288-0056, Japan

SOURCE: Life Sciences (1998), Volume Date 1999, 64(1), 45-52

CODEN: LIFSAK; ISSN: 0024-3205

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

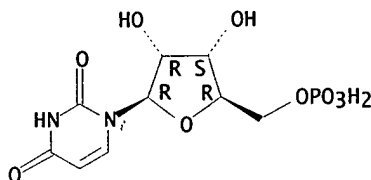
LANGUAGE: English

AB The effects of nucleotides on learning and memory were studied in normal and basal forebrain-lesioned rats using a Morris water maze test. Chronic oral administration of a nucleotide mixt. (500 mg/kg), contg. an equal wt. of the disodium salts of AMP, GMP, IMP, CMP, and UMP, facilitated learning acquisition in normal rats. In basal forebrain-lesioned rats, administration of the nucleotide mixt. showed a tendency to improve learning acquisition and memory retrieval. In the biochem. studies, no significant changes were obsd. in brain

choline and acetylcholine levels by treatment with the nucleotide mixt. at the doses tested in both normal and basal forebrain-lesioned rats. The nucleotides did not affect the monoaminergic systems in normal rats, but did cause some changes in these systems in basal forebrain-lesioned rats. The present studies indicate that nucleotides ameliorate learning and memory processes in normal rats, but not in basal forebrain-lesioned rats, and they also modulate the activity of the central monoaminergic systems under certain conditions.

IT 58-97-9, 5'-UMP, biological studies
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effects of nucleotides on learning and memory in Morris water maze test in normal and basal forebrain-lesioned rats)
 RN 58-97-9 HCAPLUS
 CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 16

L97 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
 CC 1-11 (Pharmacology)
 ST nucleotide learning memory forebrain lesion; monoaminergic system brain nucleotide
 IT Learning
 Memory, biological
 (effects of nucleotides on learning and memory in Morris water maze test in normal and basal forebrain-lesioned rats)
 IT Nucleotides, biological studies
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effects of nucleotides on learning and memory in Morris water maze test in normal and basal forebrain-lesioned rats)
 IT Neurotransmitters
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (effects of nucleotides on learning and memory in Morris water maze test in normal and basal forebrain-lesioned rats)
 IT Brain, disease
 (lesion, fore-; effects of nucleotides on learning and memory in Morris water maze test in normal and basal forebrain-lesioned rats)
 IT Brain
 (monoaminergic system; effects of nucleotides on learning and memory in Morris water maze test in normal and basal forebrain-lesioned rats)
 IT 58-97-9, 5'-UMP, biological studies 61-19-8, 5'-AMP, biological studies 63-37-6, 5'-CMP 85-32-5, 5'-GMP 131-99-7, 5'-IMP
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effects of nucleotides on learning and memory in Morris water maze test in normal and basal forebrain-lesioned rats)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies 54-16-0, 5-HIAA, biological studies 102-32-9, DOPAC 306-08-1, HVA 534-82-7, 3-Methoxy-4-hydroxy-phenylethylene glycol

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(effects of nucleotides on learning and memory in Morris water maze test in normal and basal forebrain-lesioned rats)

=> d ibib abs hitstr 17

L97 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:234128 HCAPLUS

DOCUMENT NUMBER: 126:229629

TITLE: Purine nucleosides and pyrimidine nucleosides for the treatment of memory loss

INVENTOR(S): Yamamoto, Shigeru

PATENT ASSIGNEE(S): Otsuka Pharma Co Ltd, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09030976	A2	19970204	JP 1995-179886	19950717
PRIORITY APPLN. INFO.: JP 1995-179886 19950717				

AB An agent for improving memory loss comprises a purine nucleoside and a pyrimidine nucleoside. The claimed agent contains inosine, cytidine, **uridine**, guanosine-5'-phosphate, and thymidine at the mol ratio of 4:4:3:4:1.

=> d ind 17

L97 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

IC ICM A61K031-70

ICS C07H019-067; C07H019-167; C07H019-20

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST memory improvement purine pyrimidine nucleoside; inosine cytidine **uridine** guanosine thymidine dementia

IT Drug delivery systems
(injections; memory loss treatment with purine nucleoside and pyrimidine nucleoside)

IT **Amnesia**
(memory loss treatment with purine nucleoside and pyrimidine nucleoside)

IT Purine nucleosides
Pyrimidine nucleosides

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(memory loss treatment with purine nucleoside and pyrimidine nucleoside)

IT Drug delivery systems
Drug delivery systems
(powders, oral; memory loss treatment with purine nucleoside and pyrimidine nucleoside)

IT Mental disorder
(senile psychosis; memory loss treatment with purine nucleoside and pyrimidine nucleoside)

IT 50-89-5, Thymidine, biological studies 58-63-9, Inosine 58-96-8, Uridine 65-46-3, Cytidine 85-32-5, Guanosine 5'-phosphoric acid 118-00-3, Guanosine, biological studies 5550-12-9, 5'-GMP disodium salt
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (memory loss treatment with purine nucleoside and pyrimidine nucleoside)

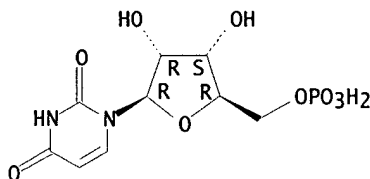
=> d ibib abs hitstr 18

L97 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1990:417462 HCAPLUS
 DOCUMENT NUMBER: 113:17462
 TITLE: Metabolization of a retention-improving dosage of methylglucamine orotate in rat brain
 AUTHOR(S): Staak, S.; Tischmeyer, W.; Popov, N.; Matthies, H.
 CORPORATE SOURCE: Inst. Neurobiol. Brain Res., Acad. Sci. GDR, Magdeburg, 3090, Ger. Dem. Rep.
 SOURCE: Biomedica Biochimica Acta (1990), 49(4), 257-62
 CODEN: BBIADT; ISSN: 0232-766X
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The present study was carried out to investigate the time course of metab. in brain and the influence on RNA synthesis of a retention-improving dosage of methylglucamine orotate after intracerebroventricular application. As detd. by the HPLC technique, 73% of acid-sol. radioactivity was recovered in unmetabolized orotic acid 30 min after injection of 1 .mu.mole methylglucamine [6-14C]orotate. Two hours later the amt. of radioactivity found in this compd. was negligible. Anal. of the sequence of labeling of uridine compds. revealed uridine to be the metabolite exhibiting the highest radioactivity at 30 min, whereas UMP- and UDP-sugars attained their max. 90 min after injection of the precursor. Incorporation of [3H]guanosine into brain RNA was not altered by intraventricular application of 1 .mu.mole methylglucamine orotate as compared to methylglucamine chloride-treated controls. The results are interpreted in the light of behavioral findings in which the pyrimidine nucleotide precursor at the dosage used improved the retention performance of an acquired behavior in the rat.

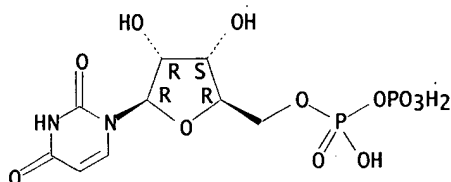
IT 58-97-9, UMP, biological studies 58-98-0, UDP, biological studies 63-39-8, UTP
 RL: BIOL (Biological study)
 (as methylglucamine orotate metabolite, in brain, memory improvement in relation to)
 RN 58-97-9, HCAPLUS
 CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



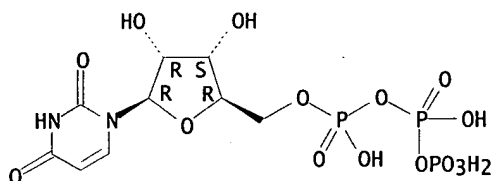
RN 58-98-0 HCAPLUS
 CN Uridine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 63-39-8 HCAPLUS
CN Uridine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr 19

L97 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1989:151896 HCAPLUS

DOCUMENT NUMBER: 110:151896

TITLE: Amnestic action of 2-deoxy-D-galactose is not related to a uridylate trapping effect

AUTHOR(S): Schmidt, S.; Richter, P.; Staak, S.; Grecksch, G.; Popov, N.; Jork, R.; Matthies, H.

CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Med. Acad., Magdeburg, 3090, Ger. Dem. Rep.

SOURCE: Neuroscience Research Communications (1989), 4(1), 1-10

CODEN: NRCOEE; ISSN: 0893-6609

DOCUMENT TYPE: Journal

LANGUAGE: English

AB When rats were trained on a brightness discrimination task, intrahippocampal injections of 2-deoxy-D-galactose caused a strong amnesia, measured as an impaired retention performance in a relearning session carried out 24 h later. This amnestic action is not related to a uridylate trapping effect induced by the deoxy-sugar, since the values of hippocampal uridine phosphates were similar to those obtained from saline-treated control animals. Therefore, the prevention of amnesia by a pretrial i.p. injection of methylglucamine orotate, known to improve long-term memory formation, seems not to be due to a substitution of trapped pyrimidine nucleotides. More likely, methylglucamine orotate accelerates the mol. mechanisms underlying the formation of a memory trace. Thus, it prevents at crit. times during memory processing those structural and(or) functional modifications of certain glycoconjugates induced by an incorporation of 2-deoxy-D-galactose into carbohydrate chains and assumed to interfere with long-term memory formation.

IT 58-97-9, 5'-UMP, biological studies 58-98-0, 5'-UDP,

biological studies 63-39-8, 5'-UTP

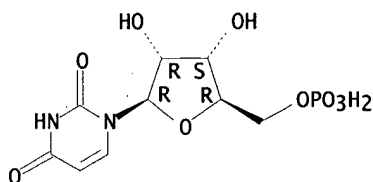
RL: BIOL (Biological study)

(of brain hippocampus, deoxygalactose effect on, long-term memory formation in relation to)

RN 58-97-9 HCAPLUS

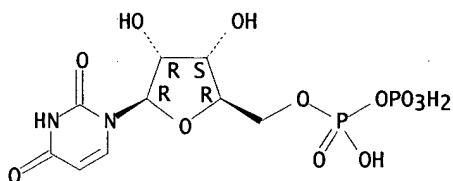
CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



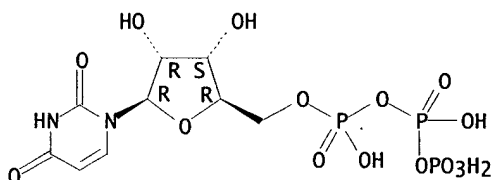
RN 58-98-0 HCAPLUS
CN Uridine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 63-39-8 HCAPLUS
CN Uridine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr 20

L97 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1974:411252 HCAPLUS

DOCUMENT NUMBER: 81:11252

TITLE: Brain uridine monophosphate. Reduced incorporation of uridine during avoidance learning

AUTHOR(S): Entingh, Dan; Damstra-Entingh, Terri; Dunn, Adrian; Wilson, John Eric; Glassman, Edward

CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, USA

SOURCE: Brain Research (1974), 70(1), 131-8

CODEN: BRREAP; ISSN: 0006-8993

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Avoidance training produced no detectable changes in the radioactivity incorporated from uridine-5-3H into total RNA of mouse brain, but decreased the radioactivity in brain UMP. The chem. response was largest in the subcortical forebrain, and did not occur in yoked control mice. This phenomenon has important implications for the interpretation of previous expts., which employed the amt. of radioactivity in UMP as the pool correction factor in studying the effects of avoidance training upon the incorporation of uridine into brain RNA.

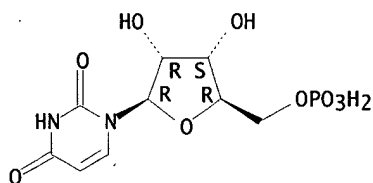
IT 58-97-9; biological studies

RL: FORM (Formation, nonpreparative)
(formation of, by brain in learning)

RN 58-97-9 HCAPLUS

CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



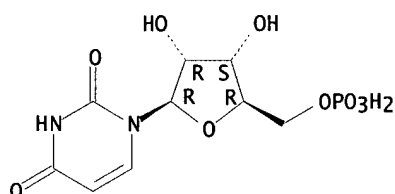
=> d ind 20

L97 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
 CC 13-2 (Mammalian Biochemistry)
 ST learning brain RNA biosynthesis; memory brain uridine metab
 IT **Learning**
 (UMP formation by brain in)
 IT Brain, metabolism
 (UMP formation by, in learning)
 IT Ribonucleic acids
 RL: FORM (Formation, nonpreparative)
 (formation of, by brain in learning)
 IT 58-97-9, biological studies
 RL: FORM (Formation, nonpreparative)
 (formation of, by brain in learning)

=> d ibib abs hitstr 21

L97 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1973:119731 HCAPLUS
 DOCUMENT NUMBER: 78:119731
 TITLE: Effects of RNA precursors on development and
 maintenance of long-term memory.
 Hippocampal and cortical pre- and post-training
 application of RNA precursors
 AUTHOR(S): Ott, Tilmann; Matthies, Hanjuergen
 CORPORATE SOURCE: Inst. Pharmakol. Toxikol., Med. Akad., Magdeburg, Ger.
 Dem. Rep.
 SOURCE: Psychopharmacologia (1973), 28(2), 195-204
 CODEN: PSYPAG; ISSN: 0033-3158
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Direct hippocampal injection of Na UMP (Na-I) [7545-48-4] (40
 .mu.g) into rats either 30 min before or 1 min after training for
 acquisition of a brightness discrimination delayed the extinction of the
 learned reaction. Hippocampal application of I 60 min after training or
 injection into the frontal cortex 30 min before the onset of training had
 no effect on the extinction. None of the types of I treatments used
 affected the acquisition capability. Thus, I may aid memory
 consolidation, possibly thru an action on RNA synthesis and subsequent
 protein synthesis. The hippocampus appears to be of importance in the
 memory consolidation process.
 IT 7545-48-4
 RL: PRP (Properties)
 (memory enhancement by hippocampal injection of)
 RN 7545-48-4 HCAPLUS
 CN 5'-Uridylic acid, sodium salt (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



●x Na

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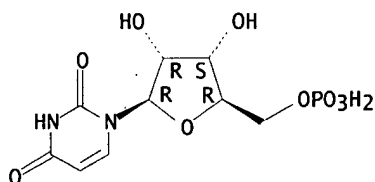
L97 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
 CC 3-5 (Biochemical Interactions)
 ST uridine memory consolidation; RNA precursor learning;
 hippocampus RNA memory; UMP memory consolidation
 IT Memory, biological
 (RNA precursor enhancement of, after hippocampal injection)
 IT Brain
 (hippocampus, in memory consolidation)
 IT Ribonucleic acids
 RL: BIOL (Biological study)
 (precursors, memory enhancement by hippocampal injection of)
 IT 7545-48-4
 RL: PRP (Properties)
 (memory enhancement by hippocampal injection of)

=> d ibib abs hitstr 22 ind

L97 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1972:149588 HCAPLUS
 DOCUMENT NUMBER: 76:149588
 TITLE: Influence of 6-azauridine on facilitation of
 relearning by precursors of ribonucleic acid
 AUTHOR(S): Ott, Tilmann; Matthies, Hansjuergen
 CORPORATE SOURCE: Inst. Pharmakol. Toxikol., Med. Akad. Magdeburg,
 Magdeburg, Ger. Dem. Rep.
 SOURCE: Psychopharmacologia (1972), 23(3), 272-8
 CODEN: PSYPAG; ISSN: 0033-3158
 DOCUMENT TYPE: Journal
 LANGUAGE: German
 AB Intraventricular injection of orotic acid [65-86-1] or UMP [58-97-9] into rats 30 min before training in a conditioned avoidance situation facilitated relearning after a retention of 24 hr. 6-Azauridine (I) [54-25-1], which inhibits the conversion of orotate to UMP, was without effect when given alone, and I did not block the action of UMP when the two were injected together. However, the facilitating effect of orotate was blocked by simultaneous treatment with I. Orotate apparently does not stimulate relearning directly but does so by supplying pyrimidine nucleotide precursors for the increased brain RNA synthesis that occurs during the consolidation of long-term memory.
 IT 58-97-9, biological studies
 RL: BIOL (Biological study)
 (memory facilitation by, azauridine effect on)
 RN 58-97-9 HCAPLUS
 CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

Copy Request



CC 3 (Biochemical Interactions)
 ST RNA synthesis brain learning; memory brain nucleic acid; orotate
 brain RNA memory; azauridine brain RNA memory; UMP
 brain RNA memory
 IT Brain, metabolism
 (RNA formation by, memory in relation to)
 IT Memory, biological
 (RNA precursors facilitation of, azauridine effect on)
 IT Ribonucleic acids
 RL: FORM (Formation, nonpreparative)
 (formation of, by brain, memory in relation to)
 IT 58-97-9, biological studies 65-86-1
 RL: BIOL (Biological study)
 (memory facilitation by, azauridine effect on)
 IT 54-25-1
 RL: PRP (Properties)
 (memory response to RNA precursors and)

=> d ibib abs hitstr 23 ind

L97 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1972:470149 HCAPLUS

DOCUMENT NUMBER: 77:70149

TITLE: Pharmacological influence on the teaching and
 memorization processes

AUTHOR(S): Matthies, Hansjuergen

CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Med. Acad., Magdeburg, Ger.
 Dem. Rep.

SOURCE: Farmakologiya i Toksikologiya (Moscow) (1972), 35(3),
 259-65

CODEN: FATOAO; ISSN: 0014-8318

DOCUMENT TYPE: Journal

LANGUAGE: Russian

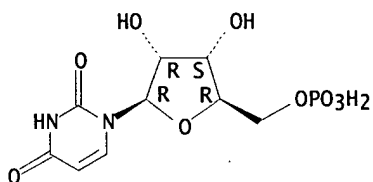
AB Orotic acid (I) [65-86-1] (100 mg/kg/day) given i.p. to rats for 14 days
 before or during elaboration of a conditional visual (brightness)
 discrimination delayed the normal extinction of learned behavior. The
 length for 50% extinction was 13 days in controls and 215 days in orotic
 acid-treated animals. This effect of orotic acid was inhibited by
 azauracil [461-89-2]. UMP [58-97-9] and CMP [63-37-6] given
 i.v. also improved memory extension even in the presence of
 azauracil, indicating that the availability of pyrimidine nucleotides in
 the brain is a limiting factor for consolidation of long-term
 memory. Trained rats incorporated more UMP into brain RNA and
 leucine into brain protein than did pseudotrained rats, confirming the
 participation of intraneuronal regulations in the consolidation of
 memory.

IT 58-97-9, biological studies
 RL: BIOL (Biological study)
 (learning and memory in response to)

RN 58-97-9 HCAPLUS

CN 5'-Uridylic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



CC 1-5 (Pharmacodynamics)
 ST orotic acid **memory**; pyrimidine nucleotide **memory**;
 learning brain protein RNA
 IT Brain, metabolism
 (RNA formation by, learning and **memory** response to
 pharmaceutical in relation to)
 IT Ribonucleic acids
 RL: FORM (Formation, nonpreparative)
 (formation of, by brain, learning and **memory** response to
 pharmaceuticals in relation to)
 IT **Learning**
Memory, biological
 (pharmaceutical effect on)
 IT 58-97-9, biological studies 63-37-6 65-86-1
 RL: BIOL (Biological study)
 (learning and **memory** in response to)
 IT 461-89-2
 RL: BIOL (Biological study)
 (learning and **memory** response to orotic acid inhibition by)